

CLAIMS

- 1) A protein or fragment thereof comprising the sequence of SEQ ID No. 1, or a functional equivalent thereof.
- 2) A protein or fragment thereof according to claim 1 which regulates the activity of a protein product of a gene in the Notch gene family.
5
- 3) A protein or fragment thereof according to claim 2 which regulates the activity of Notch 1.
- 4) A protein or fragment thereof according to either of claims 2 or 3 wherein the Notch gene is mammalian, preferably human.
- 10 5) A protein or fragment thereof according to any preceding claim which has been altered by deletion, insertion, substitution, or mutation of one or more amino acids.
- 6) A protein or fragment thereof according to any preceding claim which is recombinant.
- 7) A protein or fragment thereof according to any preceding claim that binds specifically to a member of the Notch protein family, preferably to Notch 1.
15
- 8) A protein or fragment thereof according to any preceding claim that is associated with an enzyme effector or reporter molecule.
- 9) A protein or fragment thereof according to claim 8 that is associated with a protease enzyme.
- 20 10) A protein or fragment thereof according to any preceding claim that is genetically or chemically fused to one or more peptides or polypeptides.
- 11) A protein or fragment thereof according to any preceding claim attached to a label.
- 12) A therapeutic or diagnostic composition comprising a protein or fragment thereof according to any preceding claim.

- 13) A protein or fragment thereof according to any preceding claim or composition according to claim 12 for use in therapy.
- 14) A protein or fragment thereof according to any preceding claim which for use as a pharmaceutical.
- 5 15) Use of a protein or fragment thereof according to any preceding claim as a pharmaceutical.
- 16) The use of a protein or fragment thereof according to any of claims 1-11 in the manufacture of a medicament for the treatment or prevention of cancer, or of a neurodegenerative disease.
- 10 17) A process for the identification of a compound capable of modifying the levels of expression or activity of a Notch protein comprising screening a Notchless mutant in a sensitised Notch genetic background with a candidate compound and selecting for an altered phenotype of the Notchless mutant.
- 18) A compound identified by the process of claim 17.
- 15 19) A nucleic acid sequence comprising:
- a) the sequence of SEQ ID No 2, or
 - b) a sequence that encodes on expression the amino acid sequence encoded by the sequence of part a), or
 - c) a fragment of the DNA sequence of part a) or part b) that comprises a nucleotide sequence that encodes the Notch binding domain.
- 20 20) The nucleic acid molecule of claim 19 which comprises DNA, cDNA or RNA.
- 21) A probe capable of screening for the Notchless gene, prepared from the nucleic acid sequence of claim 19.
- 22) A cloning or expression vector comprising a nucleic acid molecule according to any one of claims 19-21.
- 25

- 23) A host cell transformed or transfected with a nucleic acid according to any of claims 19-21 or with a vector according to claim 22.
- 24) A transgenic animal that has been transformed with a nucleic acid molecule according to any one of claims 19-21 or with a vector according to claim 22.
- 5 25) A method of preparing a protein or fragment thereof according to any of claims 1-11, comprising expressing a vector according to claim 22 in a host cell and culturing said host cell under conditions where said protein is expressed, and recovering said protein thus expressed.

Sequence I.D. No. 1: Drosophila Notchless protein

MQETDTEQEATPHTIQARLVYTGEAGPPIDLPAGITTQQLGLICNALLKNEEAT
PYLFFVGEDEIKSLEDTLDSLAVDTENVIDIVYQPQAVFKVRPVTRCTSSMPGHA
5 EAVVSLNFSPDGAAHLASGSGDTTVRLWDLNTETPHFTCTGHKQWVLCVSWAP
DGKRLASGCKAGSIIWDPETGQQKGRPLSGHKHHINCLAWEPYHRDPECRKL
ASASGDGDCRIWDVKGCLMNIAGHTNAVTAVRWGGAGLIYTSSKDRTVK
MWRAADGILCRTFSGHAWVNNIALSTDYVLRTGPFPVKDRSKSHLSLSTEE
LQESALKRYQAVCPEDEVESLVSCSDDNTLYLWRNNQNKCVERMTGHQNVVN
10 DVKYSPDVKLIASASFDSVRLWRASDGQYMATFRGHVQAVYTVAWSADSRL
IVSGSKDSTLVVWSVQTKKLAQELPGHADEVFGVDWAPDGSRVASGGDKVI
KLWAY

Sequence I.D. No. 2: Drosophila *Nle* cDNA

15

aattcccaaaaaATGCAGGAGACGGACACGGAGCAAGAGAGGCCACGCCACATACGA
TACAGGCGCGCCTCGTTACACGGCGAGGAAGCCGGCCGCCAATCGACC
TGCCGGCAGGAATCACTACCCAGCAATTGGACTGATTGCAACCGCCTGC
TGAAAAACGAGGAAGCCACTCCATATTGTTTTCGTGGCGAGGATGAGA
20 TCAAGAACGAGCCTGGAGGACACGTTGGACTTGGCGTCAGTGGACACCGAAA
ACGTGATCGATATTGTGTATCAGCCACAGGCCTTCAAAGTGCCTCCAGT
GACAAGATGCACGAGTCCATGCCGGACACGCCAGGGCTGTGGTTCGCT
GAATTTCAGCCCAGGATGGTGCTCATCTGCCAGTGGAAAGTGGCGACACCAC
AGTGCAGTTGTGGATCTAACACAGAGACACCGCACTTCACCTGCACAGG
25 TCATAAGCAGTGGTTCTGTGCGTATCCTGGCTCCGGATGGCAAACGGTTG
GCCAGCGGTTGCAAAGCGGGCTCTATAATCATCTGGGACCCGGAGACGGGT
CAGCAGAAGGGCGACCCCTTGAGTGGCACAAAGAAACACATCAACTGCC
GCCCTGGGAACCGTATCATCGCGATCCGGAGTGCAGGAAACTTGCTTCCGCC
AGTGGAGACGGGACTGCCGGATTGGACGTAAAATTGGGCCAGTGCCTT

ATGAAACATTGCCGGACACACAAATGCTGTGACAGCAGTGAGA~~T~~GGGGTGG
GCGGGCCTTATTATACATCCTCCAAAGATCGCACAGTGAAGATGTGGCGA
GCAGCTGATGGAATCTTGTGCCGGACGTTCTCTGGCCAAGCTCACTGGGTAA
ACAACATTGCGCTGAGCACCGATTACGTCTGCGACTGGTCCATTCCATCC
5 GGTGAAGGATCGCTCCAAGAGCCACCTCAGTTGAGCACTGAGGAATTGCA
GGAATCTGCCTTGAAGCGCTACCAGGCCGTGTGCCCTGACGAGGTGGAGTC
GCTGGTTCCCTGTTGGATGACAACACCCCTCTATCTGTGGCGAACAAACAG
AACAAAGTGCCTTGAGCGCATGACAGGGCACCAGAACGTGGTCAACGATGTG
AAATATTGCCGGATGTAAGCTAATTGCGTCTGCTTCAATTGACAAGTCAG
10 TCGTCTGTGGCGAGCCAGCGATGGTCAGTACATGCCACCTCCGGGGTC
ATGTGCAGGCTGTTACACGGTTGCCTGGTCGGACTCCGCTGATTGT
TTCCGGCAGCAAAGACTCAACTCTAAAAGTATG&AGTGTGCAGACGAAGAA
ACTGGCACAGGAGCTGCCTGGACATGCGGATGAGGTGTTGGAGTGGACTG
GGCGCCCGATGGCTCTAGAGTTGCCTCTGGTGGCAAGGACAAAGTTATAAA
15 GCTATGGGCTTATTAAcaaatcattaaacttgtacacggtaagaaaacttaggaataaagtaaaacgtcctgag
aaa

卷之三